Reactions of saccharides catalyzed by molybdate ions. XVIII.* Preparation of D-*threo*-L-talooctose and D-*erythro*-L-talooctose and their epimers

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Nitromethane synthesis with the corresponding aldoheptoses followed by oxidative decomposition of the formed sodium salts of 1-deoxy-1-nitrooctitols led to preparation of D-*erythro*-L-galactooctose, D-*erythro*-L-talooctose, D-*threo*-L-galactooctose, and D-*threo*-L-talooctose. High efficiency of the separation on a Dowex 50 W ion exchanger (in the Ba^{2+} form) of the epimeric pairs of aldoses belonging to the homomorphous series of arabinose and ribose was demonstrated in nine cases.

Нитрометановым синтезом отвечающих альдогептоз и окислительным распадом соответствующих натриевых солей 1-деокси-1-нитрооктитолов были приготовлены D-*эритро*-L-галактооктоза, D-*эритро*-L-талооктоза, D-*трео*-L-галактооктоза и D-*трео*-L-талооктоза. На примере разделения девяти эпимерных пар альдоз гомоморфного ряда арабинозы и рибозы демонстрируется высокая активность их деления на ионите Dowex 50 W в Ba^{2+} цикле.

Some of the higher monosaccharides are known to be present in various natural materials [1—3]. Since these compounds occur in the nature in very low concentrations only, their isolation and identification is associated with difficulties. In the present work we have concentrated on the preparation of some aldooctoses of the homomorphous series of ribose and arabinose and on the possibilities of their isolation and identification.

The aldooctose epimers were prepared by addition of nitromethane to D-*glycero*-D-guloheptose and/or D-*glycero*-L-mannoheptose followed by oxidative decomposition of sodium salts of the corresponding 1-deoxy-1-nitroalditols. Till now D-*threo*-L-galactooctose [4], D-*erythro*-L-galactooctose, and D-*erythro*-L-talooctose [5] have been prepared by cyanohydrin synthesis and the isolation of epimeric saccharides has been carried out at the stage of their aldonic acids. D-*threo*-L-Talooctose has not been prepared yet. Here described nitromethane synthesis is, in comparison with the cyanohydrin synthesis, substantially simplier. A good separation of epimeric aldooctoses of the homomorphous series of arabinose and ribose can be achieved on a Dowex 50 W ion exchanger using elution with water. Thus obtained talooctoses are of a high purity.

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D-*glycero*-D-Guloheptose was converted to the corresponding aldooctoses in 62% at the D-*erythro*-L-galactooctose to D-*erythro*-L-talooctose ratio 5 : 1. The conversion of D-*glycero*-L-mannoheptose was found to reach 45% at the D-*threo*-L-galactooctose to D-*threo*-L-talooctose ratio 2 : 1. The recovery of a part of the starting aldoheptoses (25% of D-*glycero*-D-guloheptose and 20% of D-*glycero*-L-mannoheptose, respectively) can be attributed to a reverse elimination reaction which accompanies the reaction of the oxidative decomposition of sodium salts of 1-deoxy-1-nitroalditols to the corresponding aldoses.

From a mixture of saccharides resulting from the isomerization of D-galactose in pyridine, *Jones* and *Wall* [6] isolated D-talose on a Dowex 50 W ion exchanger in the Ba^{2+} form. This principle of separation of aldoses of the homomorphous series of ribose was successfully applied for a larger scale separation of L-ribose from L-arabinose, L-xylose from L-lyxose [7], D-ribose from D-allose and D-altrose [8], D-talose from D-galactose, D-gulose, and D-idose [9], L-*glycero*-L-taloheptose from L-*glycero*-L-galactoheptose and L-mannose [10], 6-deoxy-D-talose from 6-deoxy-D-galactose, 6-deoxy-D-gulose, and 6-deoxy-D-idose, and 7-deoxy-

Table 1

Ion-exchange chromatography of aldoses of the homomorphous series of arabinose and ribose on a Dowex 50 W, X-8 ion exchanger in the Ba^{2+} form using elution with water. The values V_{gal} represent elution volumes of saccharides relative to that of galactose

Aldose	V_{gal}
L-*glycero*-L-Galactoheptose	0.96
D-*threo*-L-Galactooctose	0.98
D-Galactose	1.00
7-Deoxy-L-*glycero*-L-galactoheptose	1.02
D-*glycero*-L-Galactoheptose	1.04
6-Deoxy-D-galactose	1.05
L-Arabinose	1.12
5-Deoxy-L-arabinose	1.15
D-*erythro*-L-Galactooctose	1.18
L-Ribose	1.93
5-Deoxy-L-ribose	1.96
L-*glycero*-L-Taloheptose	1.98
D-Talose	2.18
D-*threo*-L-Talooctose	2.20
7-Deoxy-L-*glycero*-L-taloheptose	2.31
6-Deoxy-D-talose	2.38
D-*glycero*-L-Taloheptose	3.15
D-*erythro*-L-Talooctose	3.95

Table 2

Equilibrium mixture of the pyranoid and furanoid forms of aldoses (%) in aqueous solutions at 50°C as evaluated from the p.m.r. spectra

Aldose	β-pyr.	β-fur.	α-pyr.		α-fur.
D-Ribose*	56	18	20		6
D-Talose*	29	11	40		20
6-Deoxy-D-talose	33	17		50	
D-*glycero*-L-Taloheptose	30	15	33		22
L-*glycero*-L-Taloheptose	31	14		55	
7-Deoxy-L-*glycero*-L-taloheptose	29	15		56	
D-*erythro*-L-Talooctose	18	22	36		24
D-*threo*-L-Talooctose	39	14		47	

* Ref. [11], measured at 40°C.

-L-*glycero*-L-taloheptose from 7-deoxy-L-*glycero*-L-galactoheptose and L-rhamnose (unpublished results).

The efficiency of the separation of individual aldoses on a Dowex 50 W ion exchanger is not very significant within the homomorphous series of arabinose, however, it is more expressed in the case of the homomorphous series of ribose (Table 1). The elution volumes of aldoses did not show any correlation with their molecular weight or a number of the hydroxyl groups. As it follows from the p.m.r. spectra of aldoses of the homomorphous series of ribose (Table 2), one of the main reasons for different behaviour of individual aldoses on the ion exchanger is a considerable difference in their content of the furanoid forms. The aldooctoses prepared in this work could be efficiently separated, regardless the homomorphous series they belong to (Fig. 1).

The fact, that aldoses epimerize in acid aqueous solutions under catalytic action

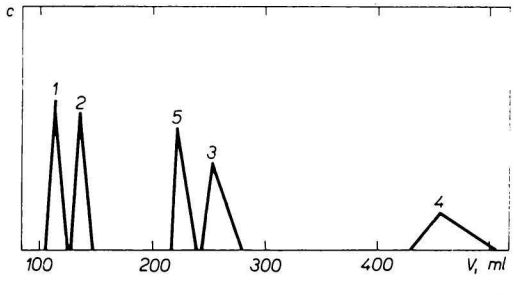

Fig. 1. Chromatographic separation of a mixture of D-*threo*-L-galactooctose (*1*), D-*erythro*-L-galactooctose (*2*), D-*threo*-L-talooctose (*3*), D-*erythro*-L-talooctose (*4*), and L-ribose (*5*) (50 mg of each) on a Dowex 50 W, X-8 ion exchanger in the Ba^{2+} form using elution with water.

of molybdate ions giving an equilibrium mixture of epimeric aldoses [8], represents an opportunity for identification of aldooctoses which is based on the proof of the formation of the complementary epimeric aldose in the epimerization reaction. In a combination with chromatographic methods, this method of identification of aldooctoses is essentially simple and not requiring larger quantities of the tested aldoses.

Experimental

Specific rotation of saccharides was measured with an automatic Perkin—Elmer polarimeter, type 141 and melting points were determined on a Kofler stage.

The p.m.r. spectra of the equilibrium anomeric forms of aldoses of the homomorphous series of ribose (Table 2) were measured on a Tesla 487 B equipment (80 MHz) in deuterium oxide at 50°C and a concentration 200 mg ml^{-1} using DSS as an internal standard. In this homomorphous series chemical shifts H-1 (p.p.m.) and interaction constants $J_{1,2}$ (Hz) showed following values: for β-pyranoid forms 4.76 ± 0.04 p.p.m. and 1.3 ± 0.1 Hz, respectively; β-furanoid forms 5.34 ± 0.04 p.p.m. and 3.9 ± 0.1 Hz; α-pyranoid forms 5.26 ± 0.07 p.p.m. and 1.6 ± 0.1 Hz; α-furanoid forms 5.21 ± 0.04 p.p.m. and 2.3 ± 0.3 Hz.

Aldoses of the homomorphous series of arabinose and ribose were chromatographed on a Dowex 50 W column (X-8, Ba^{2+} form, 100—200 mesh, 1.2×160 cm) using elution with water at a rate of 5 ± 1 ml h^{-1} (Table 1). The values V_{gal} of all aldoses are relative to the elution volume of 50 mg of galactose which occured between 111th and 122nd ml with maximum concentration of galactose in 115th ml ($V_{gal} = 1.00$). The V_{gal} values of D-*glycero*-D-guloheptose and D-*glycero*-L-mannoheptose were found to be 1.07 and 1.27, respectively.

Identification of aldooctoses by the epimerization test

An aldooctose (*ca.* 5 mg) is dissolved in 1% aqueous solution of molybdenic acid (1 ml) and heated at 100°C for 1 hr. The solution is deionized by addition of an anion exchanger and chromatographed. The chromatogram will clearly show the presence of the complementary epimeric aldose. Following R_{gal} values were observed after chromatography on Whatman No. 1 paper in *n*-butanol—ethanol—water (5:1:4): for D-*erythro*-L-galactooctose 0.52, D-*erythro*-L-talooctose 0.97, D-*threo*-L-galactooctose 0.55, and D-*threo*-L-talooctose 1.04.

Preparation of aldooctoses

Nitromethane synthesis and oxidative decomposition

Aldoheptose (D-*glycero*-D-guloheptose; 30 g) was dissolved in dimethyl sulfoxide (230 ml) or (D-*glycero*-L-mannoheptose; 30 g) in a mixture of dimethyl sulfoxide (40 ml)—methanol (190 ml). After addition of nitromethane (60 ml) and, in portions under agitation, methanol solution of sodium methoxide (7.5 g of sodium in 230 ml of methanol), the reaction mixture was left to stand at room temperature for 20 hrs. Separated sodium salts of nitrooctitols were filtered off and dissolved in 0.2% aqueous solution of sodium hydroxide (300 ml). After addition of sodium molybdate (1.5 g), 15% aqueous solution of hydrogen peroxide (60 ml) was added at a rate to keep the temperature of the reaction mixture below 30°C. The mixture was then left to stand for 24 hrs at room temperature and, after addition of 5% Pd/C (0.2 g) for another 24 hrs. Finally acetic acid was added (10 ml) and the

reaction mixture was bubbled with air for 4 hrs. The solution was deionized on ion exchangers (Wofatit KPS in the H^+ form, Wofatit SBW in the acetate form) and evaporated under reduced pressure to a syrup.

Isolation of D-*erythro*-L-*galactooctose and* D-*erythro*-L-*talooctose*

The syrupy residue (*ca.* 30 g) was crystallized from a mixture methanol (80 ml)—water (20 ml) to give a product (15 g) containing D-*erythro*-L-galactooctose and D-*glycero*-D-guloheptose in the ratio 2 : 1. The mother liquor was fractionated on a column (3.5 × 120 cm) of ion exchanger Dowex 50 W (X-8, 100—200 mesh, Ba^{2+} form) using elution with water at a rate of 45 ml h^{-1} to give a mixture of D-*erythro*-L-galactooctose and D-*glycero*-D-guloheptose in the ratio 3 : 1 (10.1 g; in the elution volume 760—1150 ml) and D-*erythro*-L-talooctose (3.7 g; 2540—3700 ml) having $[\alpha]_D^{20}$ −5.3° (*c* 3—6, water). Ref. [5] gives for D-*erythro*-L-talooctose m.p. 117—118°C and $[\alpha]_D^{20}$ −26.2° (3 min) → −7° (*c* 1.6, water).

From a mixture of D-*erythro*-L-galactooctose and D-*glycero*-D-guloheptose, the former sugar was extracted with hot methanol from which two successive crystallizations afforded chromatographically homogeneous D-*erythro*-L-galactooctose dihydrate, m.p. 96—99°C, $[\alpha]_D^{20}$ −80.5° (3 min) → −78° (5 min) → −74.0° (10 min) → −41.5° (equil.; *c* 3, water). Ref. [5] gives for D-*erythro*-L-galactooctose dihydrate m.p. 96—97°C and $[\alpha]_D^{20}$ −77.5° (10 min) → −44.6° (equil.; *c* 2, water).

Isolation of D-*threo*-L-*galactooctose and* D-*threo*-L-*talooctose*

The syrupy residue obtained after oxidative decomposition and deionization (22 g) was fractionated on Dowex 50 W ion exchanger as described in the case of the isolation of the isomeric aldooctoses. This step afforded D-*threo*-L-galactooctose (7.4 g in the elution volume 630—910 ml), a mixture of D-*threo*-L-galactooctose and D-*glycero*-L-mannoheptose in the ratio 2 : 1 (4.7 g; 910—1050 ml), D-*glycero*-L-mannoheptose (4.4 g, 1050—1400 ml), and D-*threo*-L-talooctose (4.8 g; 1600—2000 ml).

Crystallization from a mixture water—methanol (1 : 1) gave D-*threo*-L-galactooctose monohydrate, m.p. 98—101°C → 164—169°C, $[\alpha]_D^{20}$ −37.4° (5 min) → −53.6° (24 hrs, *c* 2, water). Ref. [4] gives for D-*threo*-L-galactooctose m.p. 167—169°C and $[\alpha]_D^{20}$ −44.9° (3 min) → −61.7° (equil.; *c* 0.8, water), and for its monohydrate m.p. 103°C → 167—169°C and $[\alpha]_D^{20}$ −40.0° (5 min) → −56.8° (equil.; *c* 4, water).

D-*threo*-L-Talooctose was obtained by crystallization from anhydrous methanol. The product showed m.p. 138—140°C and $[\alpha]_D^{20}$ −25.7° (extrapol.) −22.2° (2 min) → −18.0° (4 min) → −16.4° (6 min) → −15.7° (8 min) → −15.1° (10 min) → −14.4° (equil.; *c* 3, water).

For $C_8H_{16}O_8$ calculated: 40.00% C, 6.71% H; found: 39.84% C, 6.75% H.

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